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Predictors of Cardiogenic Shock After Thrombolytic Therapy for Acute Myocardial Infarction

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OBJECTIVES This study characterized clinical factors predictive of cardiogenic shock developing after thrombolytic therapy for acute myocardial infarction (AMI).

BACKGROUND Cardiogenic shock remains a common and ominous complication of AMI. By identifying patients at risk of developing shock, preventive measures may be implemented to avert its development.

METHODS We analyzed baseline variables associated with the development of shock after thrombolytic therapy in the Global Utilization of Streptikonase and Tissue-Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) trial. Using a Cox proportional hazards model, we devised a scoring system predicting the risk of shock. This model was then validated in the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO-III) cohort.

RESULTS Shock developed in 1,889 patients a median of 11.6 h after enrollment. The major factors associated with increased adjusted risk of shock were age (χ^2 = 285, hazard ratio [95% confidence interval] 1.47 [1.40, 1.53]), systolic blood pressure (χ^2 = 280), heart rate (χ^2 = 225) and Killip class (χ^2 = 161, hazard ratio 1.70 [1.52, 1.90] and 2.95 [2.39, 3.63] for Killip II versus I and Killip III versus I, respectively) upon presentation. Together, these four variables accounted for >85% of the predictive information. These findings were transformed into an algorithm with a validated concordance index of 0.758. Applied to the GUSTO-III cohort, the four variables accounted for >95% of the predictive information, and the validated concordance index was 0.796.

CONCLUSIONS A scoring system accurately predicts the risk of shock after thrombolytic therapy for AMI based primarily on the patient's age and physical examination on presentation. (J Am Coll Cardiol 2000;35:136–43) © 1999 by the American College of Cardiology

Cardiogenic shock remains a relatively common complication of acute myocardial infarction (AMI), still portending an ominous prognosis despite the advent of new or refined therapeutic strategies (1–18). By identifying patients at risk for developing cardiogenic shock, preventive measures may be implemented in an attempt to avert the development of shock. The aim of the current study was to develop a model to predict the occurrence of cardiogenic shock among patients with AMI receiving thrombolytic therapy in the Global Utilization of Streptokinase and Tissue-Plasminogen Activator for Occluded Coronary Arteries-I (GUSTO-I) trial (19) and to validate it in another large cohort of patients receiving thrombolytic therapy for AMI.

METHODS

The details and results of the GUSTO-I trial have been previously reported (19). In brief, 41,021 patients from 15 countries presenting within 6 h of the onset of chest pain with typical electrocardiographic (ECG) changes (>0.1 mV ST-segment elevation in ≥2 limb leads or >0.2 mV in ≥2 precordial leads) were eligible for randomization to one of four intravenous (IV) thrombolytic strategies: 1) streptoki-

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Abbreviations and Acronyms

AMI	=	acute myocardial infarction
CI	=	confidence interval
ECG	=	electrocardiographic
GUSTO-I	=	Global Utilization of Streptokinase and Tissue-Plasminogen Activator for Occluded Coronary Arteries
GUSTO-III	=	Global Use of Strategies to Open Occluded Coronary Arteries

nase (Kabikinase, Kabi Vitrum, Stockholm, Sweden), 1.5 million U over 1 h, with subcutaneous heparin; 2) streptokinase with IV heparin; 3) accelerated recombinant tissue-type plasminogen activator (Activase, Genentech, South San Francisco, California), 15 mg bolus followed by infusion at 0.75 mg/kg (≤50 mg) for 30 min and 0.5 mg/kg (≤35 mg) over the next hour, and IV heparin; 4) tissue-type plasminogen activator (1.0 mg/kg over 1 h (≤90 mg)) and streptokinase (1 million U over 1 h) with IV heparin. Adjunctive therapy included chewable aspirin (≥160 mg; Bayer) followed by 160 to 325 mg/day, and IV atenolol (10 mg; ICI Pharmaceuticals, Wilmington, Delaware) followed by daily oral therapy (50 to 100 mg).

Other medications were given at the discretion of the attending physician. Angiography, right-heart catheterization, percutaneous coronary revascularization, intraaortic balloon pumping and coronary bypass surgery were also used at the discretion of the attending physician.

Patients with cardiogenic shock were prospectively identified (5,15,16,18). Cardiogenic shock was defined as systolic blood pressure <90 mm Hg for ≥1 h that was not responsive to fluid administration alone, thought to be secondary to cardiac dysfunction, and associated with signs of hypoperfusion or cardiac index ≤2.2 liters/min/mm^2 and pulmonary capillary wedge pressure >18 mm Hg. Patients in whom systolic blood pressure increased to >90 mm Hg within 1 h after administration of positive inotropic agents, or patients who died within 1 h of hypotension but met other criteria for cardiogenic shock, were still classified as having cardiogenic shock. In the current analysis we excluded patients who presented with shock or who were missing precise data as to the timing of shock relative to the time of enrollment. To characterize the temporal relationship of shock to thrombolytic therapy, the occurrence of shock was also analyzed based on its timing after enrollment: ≤1 h, >1 to 2 h, >2 to 6 h, >6 to 24 h, >24 to 48 h, and >48 h.

Statistical analysis. Continuous variables are presented as medians with 25th and 75th percentiles and discrete variables as frequencies and percentages. Multivariable Cox proportional hazards survival modeling techniques were used to develop a model to predict the time to in-hospital cardiogenic shock. Missing characteristics were imputed for all patients with partial data using a method for simultaneous imputation and transformation of predictor variables based on the concepts of maximum generalized variance and canonical variables (20). A backward-elimination method was used to determine the significant predictors in the model (elimination criterion, $p > 0.05$). Because the precise timing was not available for invasive procedures such as angioplasty or intraaortic balloon counterpulsation, we did not include these variables in our analyses. Predictors in the above models were tested using the Wald chi-square test. Results are also presented as hazard ratios and 95% confidence intervals (CI). Once the final model was developed, bootstrapping was used (21,22) for internal validation (100 bootstrapping samples). The quality of the final model based on the original as well as the bootstrapped samples is described with the use of the concordance index, which is a description of the discriminant power of the model to reliably predict an outcome (23).

On the basis of the coefficients in the model, a probability chart was developed for the occurrence of shock in-hospital. As we previously described (18), each variable in the model received a certain score based on the value of the variable. The total points were then transformed into predictive values.

Validation. For verification purposes, the model we developed in the GUSTO-I cohort was used in the Global Use of Strategies to Open Occluded Coronary Arteries III (GUSTO-III) cohort (24). In GUSTO-III, 30-day outcome of patients randomized to receive either reteplase or alteplase was equivalent. We have previously reported that treatment with alteplase versus reteplase did not have an effect on the occurrence or the outcome of shock in GUSTO-III (25).

Of the 15,058 patients enrolled in GUSTO-III, we eliminated 83 from this analysis because they presented with shock and an additional 15 because we were unable to determine from available data when they developed shock; this left a modeling sample of 14,960 patients. We tested the GUSTO-I shock model in this GUSTO-III population, of whom 643 patients developed cardiogenic shock after enrollment.

RESULTS

Patient population. Of the 41,021 patients enrolled in the GUSTO-I trial, data regarding shock status were missing for 305. Of the remaining 40,716 patients, 680 were excluded because they developed shock prior to enrollment, and 383 were excluded because they had severe hemodynamic compromise after enrollment but did not meet our strict criteria for shock. This analysis pertains to the 1,889 patients who unequivocally developed shock after admission.

Time to shock. The median time from enrollment to shock was 11.6 (2.2, 41.9) h. Shock developed within 6 h of enrollment in 39.6% of shock patients and within 24 h in

Table 1. Baseline Characteristics by Shock Group

Characteristic	Developed Shock						All Shock (n = 1,889)	No Shock (n = 37,764)	p-Value*
	≤1 h (n = 282)	>1 to 2 h (n = 159)	>2 to 6 h (n = 293)	>6 to 24 h (n = 437)	>24 to 48 h (n = 248)	>48 h (n = 433)			
Age (yrs)	67 (58, 72)	67 (59, 75)	67 (57, 76)	69 (60, 76)	70 (62, 76)	70 (62, 76)	69 (60, 75)	61 (52, 69)	0.001
Female	104 (36.9)	60 (37.7)	110 (37.5)	160 (36.6)	102 (41.1)	151 (34.9)	701 (37.1)	9,136 (24.2)	0.741
Smoking history									0.006
Current	107 (39.8)	61 (40.7)	93 (32.9)	145 (33.6)	68 (28.2)	121 (28.5)	602 (32.8)	16,428 (43.8)	
Former	62 (23.0)	30 (20.0)	90 (31.8)	135 (31.3)	72 (29.9)	137 (32.2)	536 (29.2)	10,262 (27.3)	
Never	100 (37.2)	59 (39.3)	100 (35.3)	151 (35.0)	101 (41.9)	167 (39.3)	696 (37.9)	10,845 (28.9)	
Hypertension	138 (49.5)	51 (32.3)	124 (42.3)	181 (41.5)	115 (46.4)	199 (46.3)	821 (43.7)	14,157 (37.6)	0.009
Diabetes	45 (16.2)	26 (16.5)	51 (17.5)	84 (19.3)	43 (17.3)	85 (19.8)	345 (18.4)	5,415 (14.4)	0.804
Family history	97 (40.2)	61 (43.3)	96 (35.6)	144 (36.2)	93 (39.7)	162 (40.5)	667 (38.9)	15,466 (42.4)	0.504
Hyperlipidemia	84 (32.3)	48 (33.3)	100 (36.0)	125 (30.3)	61 (25.4)	135 (32.9)	566 (31.8)	12,672 (34.5)	0.173
Previous MI	68 (24.5)	41 (26.5)	67 (23.1)	102 (23.5)	55 (22.2)	117 (27.0)	456 (24.3)	5,909 (15.7)	0.692
Previous angina	118 (42.6)	62 (40.3)	114 (39.3)	171 (39.7)	106 (43.1)	208 (48.3)	789 (42.3)	13,722 (36.5)	0.118
Previous PTCA	13 (4.6)	2 (1.3)	8 (2.8)	13 (3.0)	8 (3.2)	18 (4.2)	63 (3.4)	1,524 (4.0)	0.375
Previous CABG	22 (7.8)	10 (6.3)	8 (2.7)	24 (5.5)	19 (7.7)	45 (10.4)	131 (6.9)	1,567 (4.2)	0.002
Killip class									0.061
I	200 (71.4)	102 (64.2)	192 (66.0)	314 (72.2)	180 (73.5)	308 (71.5)	1,321 (70.3)	32,903 (87.1)	
II	57 (20.4)	50 (31.4)	80 (27.5)	101 (23.2)	58 (23.7)	99 (23.0)	455 (24.2)	4,480 (11.9)	
III	23 (8.2)	7 (4.4)	19 (6.5)	20 (4.6)	7 (2.9)	24 (5.6)	102 (5.4)	381 (1.0)	
US Location	202 (71.6)	91 (57.2)	180 (61.4)	271 (62.0)	149 (60.1)	269 (62.1)	1,190 (63.0)	20,992 (55.6)	0.023
Height (cm)	170 (163, 178)	170 (162, 175)	170 (162, 178)	170 (162, 175)	170 (160, 177)	170 (162, 177)	170 (162, 177)	172 (165, 178)	0.291
Weight (kg)	77 (66, 89)	72 (65, 82)	75 (66, 86)	74 (65, 84)	75 (65, 83)	73 (65, 83)	75 (65, 85)	79 (70, 89)	0.015
MI location									< 0.001
Anterior	106 (37.7)	72 (45.3)	134 (46.0)	262 (60.0)	161 (64.9)	234 (54.2)	988 (52.4)	14,371 (38.2)	
Inferior	167 (59.4)	84 (52.8)	149 (51.2)	163 (37.3)	78 (31.5)	192 (44.4)	851 (45.1)	21,977 (58.4)	
Other	8 (2.8)	3 (1.9)	8 (2.7)	12 (2.7)	9 (3.6)	6 (1.4)	46 (2.4)	1,313 (3.5)	
Systolic BP (mm Hg)	105 (90, 121)	113 (98, 130)	120 (104, 130)	120 (108, 137)	121 (110, 140)	124 (110, 140)	120 (104, 135)	130 (114, 145)	< 0.001
Diastolic BP (mm Hg)	67 (55, 78)	70 (60, 80)	71 (63, 82)	76 (65, 89)	78 (66, 85)	77 (68, 85)	73 (63, 84)	80 (70, 90)	< 0.001
Heart Rate (beats/min)	78 (62, 97)	80 (65, 95)	82 (70, 96)	80 (69, 94)	80 (68, 94)	77 (66, 90)	80 (67, 94)	73 (62, 85)	0.019
Treatment									0.129
tPA	47 (16.7)	32 (20.1)	57 (19.5)	76 (17.4)	58 (23.4)	107 (24.7)	387 (20.5)	9,680 (25.6)	
SK-IV	77 (27.3)	48 (30.2)	77 (26.3)	129 (29.5)	72 (29.0)	113 (26.1)	525 (27.8)	9,549 (25.3)	
Combo	67 (23.8)	43 (27.0)	27 (25.3)	113 (25.9)	49 (19.8)	113 (26.1)	466 (24.7)	9,560 (25.3)	
SK-SQ	91 (32.3)	36 (22.6)	85 (29.0)	119 (27.2)	69 (27.8)	100 (23.1)	511 (27.1)	8,975 (23.8)	
Received Tx	273 (96.8)	155 (97.5)	289 (98.6)	426 (97.9)	241 (97.2)	427 (98.6)	1,844 (97.7)	37,161 (98.5)	0.520
Given Tx per protocol	179 (66.3)	120 (77.9)	233 (82.9)	346 (81.4)	200 (83.7)	349 (82.1)	1,450 (79.4)	31,087 (84.6)	< 0.001
Time to treatment (h)	2.7 (1.8, 3.6)	2.8 (2.1, 4.2)	2.8 (2.1, 4.0)	3.0 (2.0, 4.2)	3.2 (2.2, 4.6)	3.1 (2.3, 4.2)	3.0 (2.1, 4.1)	2.8 (2.0, 3.9)	0.001

*p-Value for testing for differences across the timing of shock categories.

We could not determine the exact time to shock in 37 patients who developed shock after enrollment, although the data were recorded. These patients were excluded from the timing breakdown but were included in the overall numbers.

MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass grafting surgery; BP = blood pressure; tPA = tissue-plasminogen activator; SK = streptokinase; IV = intravenous; Combo = combination of tissue-plasminogen activator and streptokinase; SQ = subcutaneous; Tx = thrombolytic therapy; US = patients enrolled in the U.S.

63.2% (Table 1). The vast majority of shock patients (97.7%) received thrombolytic therapy, although only 79.4% received such treatment as stipulated by the protocol. The median time from onset of symptoms to treatment was 3.0 (2.1, 4.1) h for the shock patients.

Baseline characteristics. In general, the patients who developed shock after enrollment were older than nonshock patients and were more commonly women. The shock patients also had more co-morbid conditions such as hypertension and diabetes mellitus, but they were less frequently cigarette smokers. More shock patients had experienced a prior infarction. The physical examination revealed that more shock patients arrived with Killip classes II and III and that upon presentation their systemic blood pressure was lower and their heart rate higher.

There were several differences in baseline characteristics among the various shock groups categorized based on the timing of shock (Table 1). Shock developed earlier in younger patients who were more commonly cigarette smokers and more frequently had inferior wall AMI. The patients with early shock had lower blood pressure upon presentation without a significant difference in heart rate or Killip class.

Model. In the Cox proportional hazards survival model (Table 2), the major factors associated with increased adjusted risk of shock were age (χ^2 = 285, hazard ratio and 95% CI of 1.47 [1.40, 1.53]), as well as systolic blood pressure (χ^2 = 280), heart rate (χ^2 = 225) and Killip class (χ^2 = 161, hazard ratio of 1.70 [1.52, 1.90] and 2.95 [2.39, 3.63] for Killip class II vs. class I and Killip class III vs. Class I, respectively) upon presentation. Together, these four variables provided >85% of the information needed to predict the occurrence of shock.

The relationship between age, weight, and diastolic blood pressure and developing shock was linear. The relationship between the systolic blood pressure and heart rate and developing shock was more complex, as is evident in Figures 1 and 2, respectively.

Algorithm. We converted the results of the model into a scoring system algorithm (Table 3). Based on certain categorical clinical features such as prior AMI or gender, as well as the value of continuous variables such as age or systolic blood pressure upon presentation, a composite score can be calculated. This composite score can then be used to estimate the risk of developing shock after thrombolytic therapy.

Validation. The same four variables as in the GUSTO-I model were significant in the GUSTO-III population: age (χ^2 = 96, hazard ratio of 1.49 [1.38, 1.62]), systolic blood pressure (χ^2 = 138), heart rate (χ^2 = 94) and Killip class (χ^2 = 82; hazard ratio of 2.0 [1.65, 2.43] and hazard ratio of 3.34 [2.43, 4.61] for Killip class II vs. class I and Killip class III vs. class I, respectively). These four variables accounted for >95% of the predictive information in the GUSTO-III population. The validated concordance index was 0.796.

Table 2. Baseline Independent Predictors of Developing Cardiogenic Shock

Characteristic	Wald χ^2	*df*	p-Value	Hazard Ratio	95% CI
Age	285.14	1	< 0.001	1.47*	(1.40, 1.53)
Systolic BP	279.55	2	< 0.001		
Heart rate	225.28	3	< 0.001		
Killip class	161.35	2	< 0.001		
II vs. I				1.70	(1.52, 1.90)
III vs. I				2.95	(2.39, 3.63)
MI location	77.05	2	< 0.001		
Anterior vs. other				1.62	(1.21, 2.15)
Inferior vs. other				1.07	(0.80, 1.43)
U.S.	43.92	1	< 0.001	1.39	(1.26, 1.53)
Treatment	36.87	3	< 0.001		
SK-IV vs. tPA				1.39	(1.22, 1.59)
Combo vs. tPA				1.22	(1.07, 1.40)
SK-SQ vs. tPA				1.46	(1.28, 1.66)
Previous MI	25.61	1	< 0.001	1.34	(1.20, 1.50)
Previous CABG	15.38	1	< 0.001	1.46	(1.21, 1.76)
Weight	13.65	1	< 0.001	0.94*	(0.91, 0.97)
Female	12.69	1	< 0.001	1.22	(1.09, 1.35)
Hypertension	8.42	1	0.004	1.15	(1.05, 1.26)
Previous PTCA	7.31	1	0.007	0.70	(0.54, 0.91)
Diastolic BP	5.73	2	0.017	1.06*	(1.01, 1.11)

*Hazard ratio is for an increase of 10 U. The hazard ratios are not presented for heart rate and BP because the relationship was nonlinear.

Overall model χ^2 = 1,789 with 21 *d.f.*, n = 38,942 with 1,889 events Concordance index = 0.761, validated model = 0.758. The variables included in the model are listed in Table 1.

CI = confidence interval; BP = blood pressure; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass grafting surgery; tPA = tissue-plasminogen activator; SK = streptokinase; IV = intravenous; Combo = combination of tissue-plasminogen activator and streptokinase; SQ = subcutaneous.

DISCUSSION

Current therapeutic approaches to cardiogenic shock remain of limited efficacy. Even using aggressive revascularization interventions, short-term mortality has reached >70% in recent series of shock patients (8,17). In the absence of overwhelmingly effective treatments for shock, an alternative approach is to identify patients at high risk for developing shock and to attempt to avert its development. In the present study we identified 1,889 patients who developed cardiogenic shock after they were enrolled and who were randomized to various thrombolytic therapies in the GUSTO-I trial. Using this population, we developed a model to predict the occurrence of shock. To validate it, we applied it to the GUSTO-III patient population.

Predictors of shock. Our findings demonstrate that certain demographic and clinical parameters are strongly associated with the development of shock after thrombolytic therapy. Older age was the variable most strongly associated with the occurrence of shock: for every 10-year increase in age, the

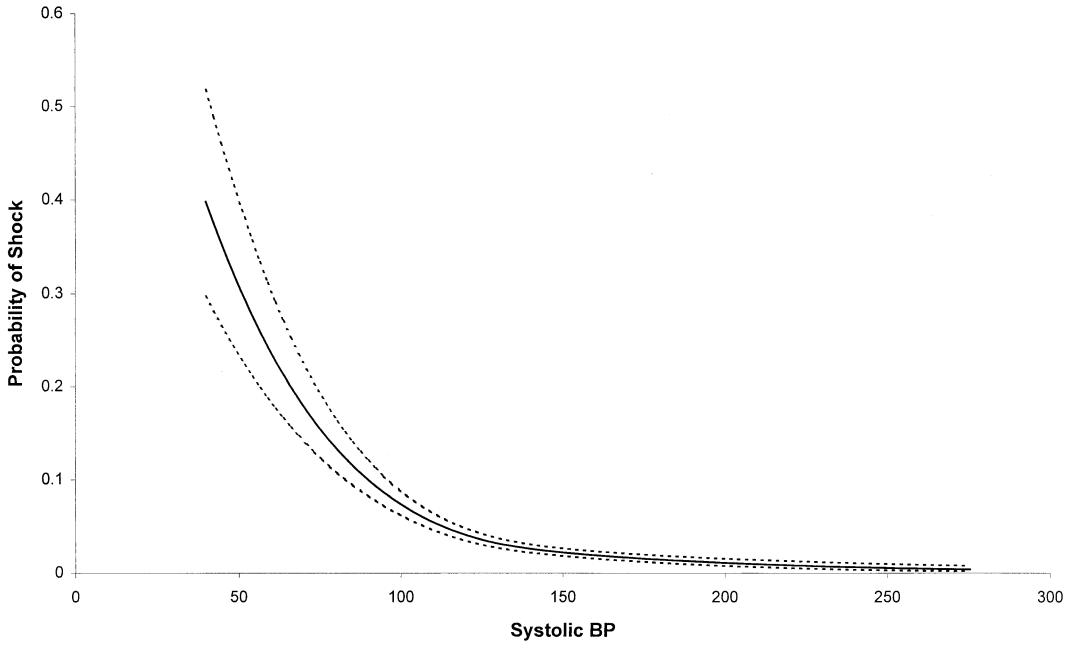

Figure 1. The relationship between systolic blood pressure (BP) upon presentation and the probability of shock developing after thrombolytic therapy.

risk of developing shock was greater by 47%. In addition, simple parameters derived from the physical examination, such as systolic blood pressure, heart rate and Killip class among patients who did not present with shock, were strong predictors of shock developing subsequently. Together, the patient's age and these physical parameters provided >85% of the information needed to predict shock in our model. These variables have also been shown to be major predictors of 30-day mortality in an analysis of the entire GUSTO-I cohort (26).

Comparison with prior studies. Leor et al. (27) previously reported that in the prethrombolysis era, among patients

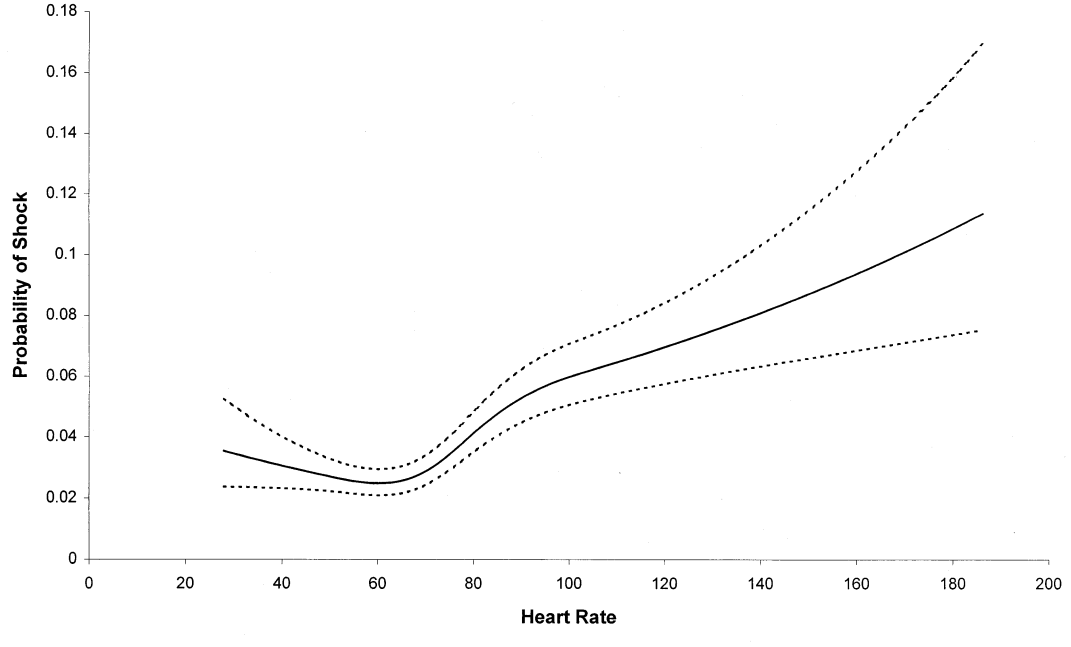

Figure 2. The relationship between heart rate upon presentation and the probability of shock developing after thrombolytic therapy.

Table 3. Baseline Predictors of Cardiogenic Shock

1. Find points for each predictive factor

Age		Heart Rate (HR)		Systolic BP		Diastolic BP	
Yrs	**Points**	**Beats/min**	**Points**	**mm Hg**	**Points**	**mm Hg**	**Points**
20	6	40	3	80	59	40	4
30	12	60	0	100	49	60	5
40	19	80	8	120	39	80	7
50	25	100	14	140	32	100	9
60	31	120	17	160	27	120	11
70	37	140	19	180	23	140	13
80	43	160	22	200	18	160	15
90	49	180	24	220	14	180	16
		200	27	240	9	200	18
		220	29	260	5		
		240	32	280	0		
		260	34				

Weight		Treatment		Killip Class	
kg	**Points**	**Tx**	**Points**	**Class**	**Points**
40	19	TPA	0	I	0
60	17	SK-IV	5	II	9
80	15	Combo	3	III	17
100	12	SK-SQ_	6		
120	10				
140	8	MI Location		Miscellaneous Risk Factors	
160	6			Previous MI	5
180	4	Ant.	8	Previous CABG	6
200	2	Inf.	1	No previous PTCA	6
220	0	Other	0	Female	3
				Hypertension	2
				US	5

2. Sum points for all predictive factors:

Age	HR	+	Sys BP	+	Dia BP	+	Wgt	+	Tx	+	MI loc	+	Killip Class	Msc	=	Total Pts

3. Look up risk corresponding to total points:

Points	Probability of In-hospital Cardiogenic Shock
92	1%
103	2%
110	3%
114	4%
118	5%
130	10%
137	15%
142	20%
146	25%
149	30%
152	35%
155	40%
158	45%
160	50%

In panel 1, find the value most closely matching the patient's risk factors and circle the points. In panel 2, sum the points for all predictive factors. In panel 3, determine the predicted occurrence of cardiogenic shock corresponding to the total number of points. For example, a 71-year-old 60-kg female from the U.S. with a history of hypertension, who presents with a systolic blood pressure of 126 mm Hg, a diastolic blood pressure of 64 mm Hg, a heart rate of 123 beats/min, in Killip class III, and an anterior myocardial infarction who was then treated with intravenous streptokinase, would have a total score of (37+17+39+5+10+5+8+17+[3+2+5]) = 148. This score corresponds to predicted probability of 30% for cardiogenic shock occurring after thrombolytic therapy.

BP = blood pressure; MI = myocardial infarction; Tx = thrombolytic therapy; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary artery bypass grafting surgery; tPA = tissue-plasminogen activator; SK = streptokinase; IV = intravenous; Combo = combination of tissue-plasminogen activator and streptokinase; SQ_= subcutaneous; US = patients enrolled in the U.S.; Wght = weight.

with AMI without clinical signs of heart failure upon presentation, cardiogenic shock developed in-hospital in 89 (2.6%) of 3,465 patients. Among the independent predictors for in-hospital shock were older age, female sex, prior angina, prior stroke and peripheral vascular disease. Hands et al. (28) reported that shock developed in 60 (7.1%) of 845 patients admitted with AMI also in the prethrombolysis era. Independent predictors of the occurrence of shock were age >65 years, left ventricular ejection fraction <35%, larger infarct as estimated by serial enzyme determinations, prior AMI and diabetes mellitus. In these earlier studies (27,28), parameters from the physical examination were not included in the analysis.

Our study of 1,889 patients who developed shock after thrombolytic therapy complements these prior studies, demonstrating again the strong association between increased age and the occurrence of shock. Moreover, our study underscores the importance of the physical examination; variables easily derived from the physical examination were of much greater significance in predicting the occurrence of shock than other variables such as prior AMI or infarct location. Similarly, we have recently demonstrated that other variables derived from the physical examination such as altered sensorium, oliguria and cold, clammy skin were of great significance in predicting death among patients with shock (18).

Timing of shock. The challenge for the clinician is to promptly and thoroughly identify the patient at risk for developing shock and to avert this complication. In the prethrombolysis era, Leor et al. (27) reported that shock developed at a mean of 4 ± 4 days after admission (median two days, range 3 h to 16 days) in patients who were admitted with Killip class I, and Hands et al. (28) reported that shock occurred at a mean of 3.4 ± 0.8 days (with half the patients developing shock within the first 24 h) in patients who did not have shock upon admission. More recent data have stressed the earlier occurrence of shock (7,12); shock occurred at a median of 9 h after onset of AMI. In GUSTO-I, we observed that among patients who did not present with shock and who received thrombolytic therapy, shock developed at a median of 11.6 h. Moreover, shock developed within 6 h in 39.6% of shock patients and within 24 h in 63.2% of such patients. These data indicate that the window of opportunity to attempt to avert the development of shock is very short-lived; patients must be identified and measures should be taken within hours of presentation.

Study limitations. There are several caveats to consider in interpreting our results. First, our analysis pertains only to patients who did not die or develop shock before arrival at the hospital and who were well enough to sign a written informed consent to participate in a randomized trial. Moreover, this cohort included only patients with ST-segment elevation upon presentation who were eligible for thrombolytic therapy. Second, some of the patients who came in with a low blood pressure may have been in subclinical shock. However, the study protocol also required that the hypotension be accompanied by signs of hypoperfusion to define shock. Apparently the attending physicians did not consider these patients to be in cardiogenic shock using our definition.

Third, in the current study we identified patients at risk of developing shock but did not prove that it is possible to avert the occurrence of shock after thrombolytic therapy. Although thrombolytic therapy in itself has reduced the occurrence of shock (29,30), there is no evidence as yet that other measures after thrombolytic therapy influence the development of shock. However, revascularization after thrombolytic therapy may be of value in high-risk populations, in contrast to its lack of effect when applied indiscriminately (31,32). Unfortunately, in current clinical practice, revascularization is more commonly offered to lower-risk patients (33–35).

In addition, the administration of therapeutic agents that improve cardiac myocyte metabolism, such as IV glucose-insulin-potassium solutions (36), may prove to be salutary. Studies investigating the efficacy of aggressive revascularization or other measures after thrombolytic therapy in preventing shock in high-risk subpopulations, such as those identified by our model, are warranted.

Conclusions. We devised a simple scoring system to predict the risk of cardiogenic shock occurring after thrombolytic therapy, and we validated it in an independent cohort. Based primarily on the age of the patient and findings easily derived from the physical examination upon presentation, it is possible to estimate with accuracy the risk of shock. The physician attending to the patient with AMI now faces the challenge of promptly identifying the patient at risk and taking measures to avert the occurrence of shock.

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